

FIG. 1

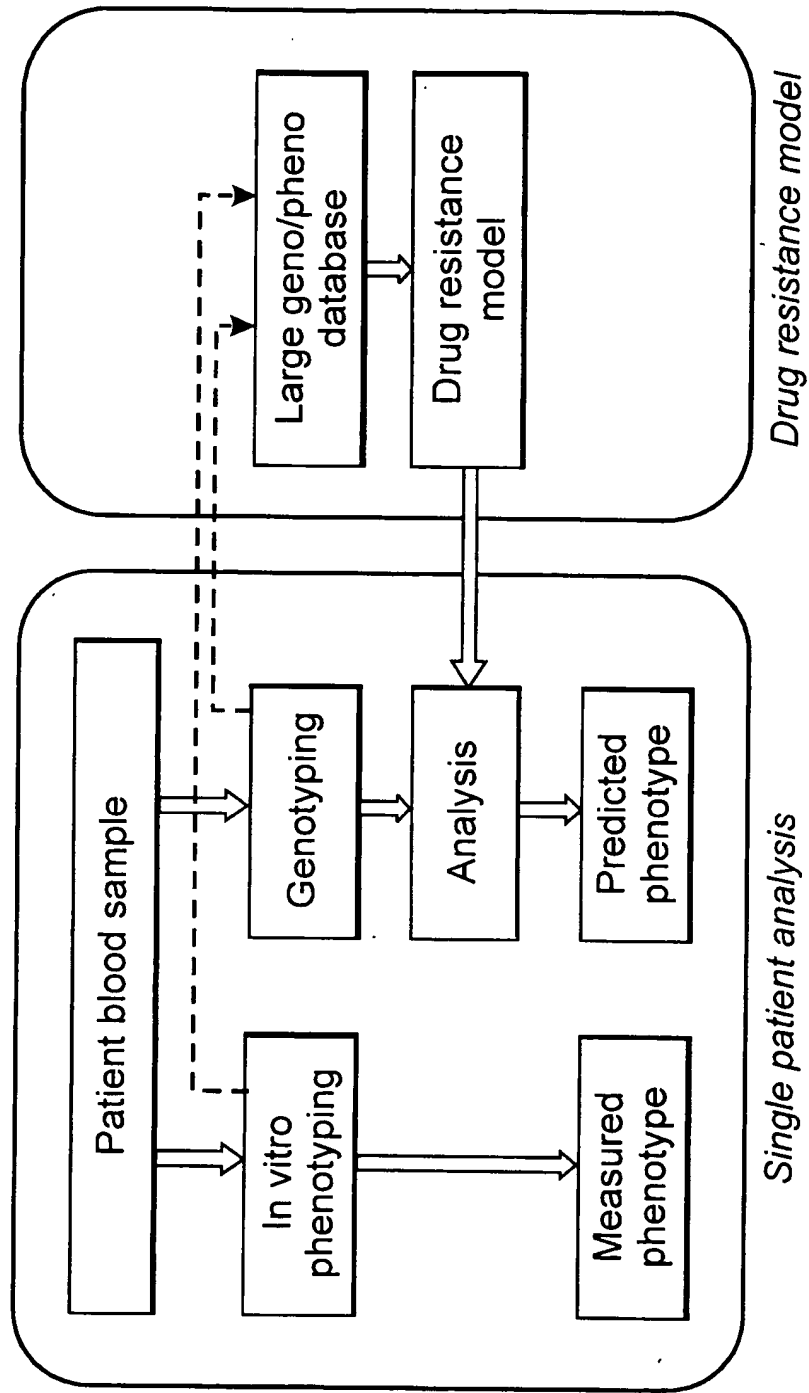


FIG. 2

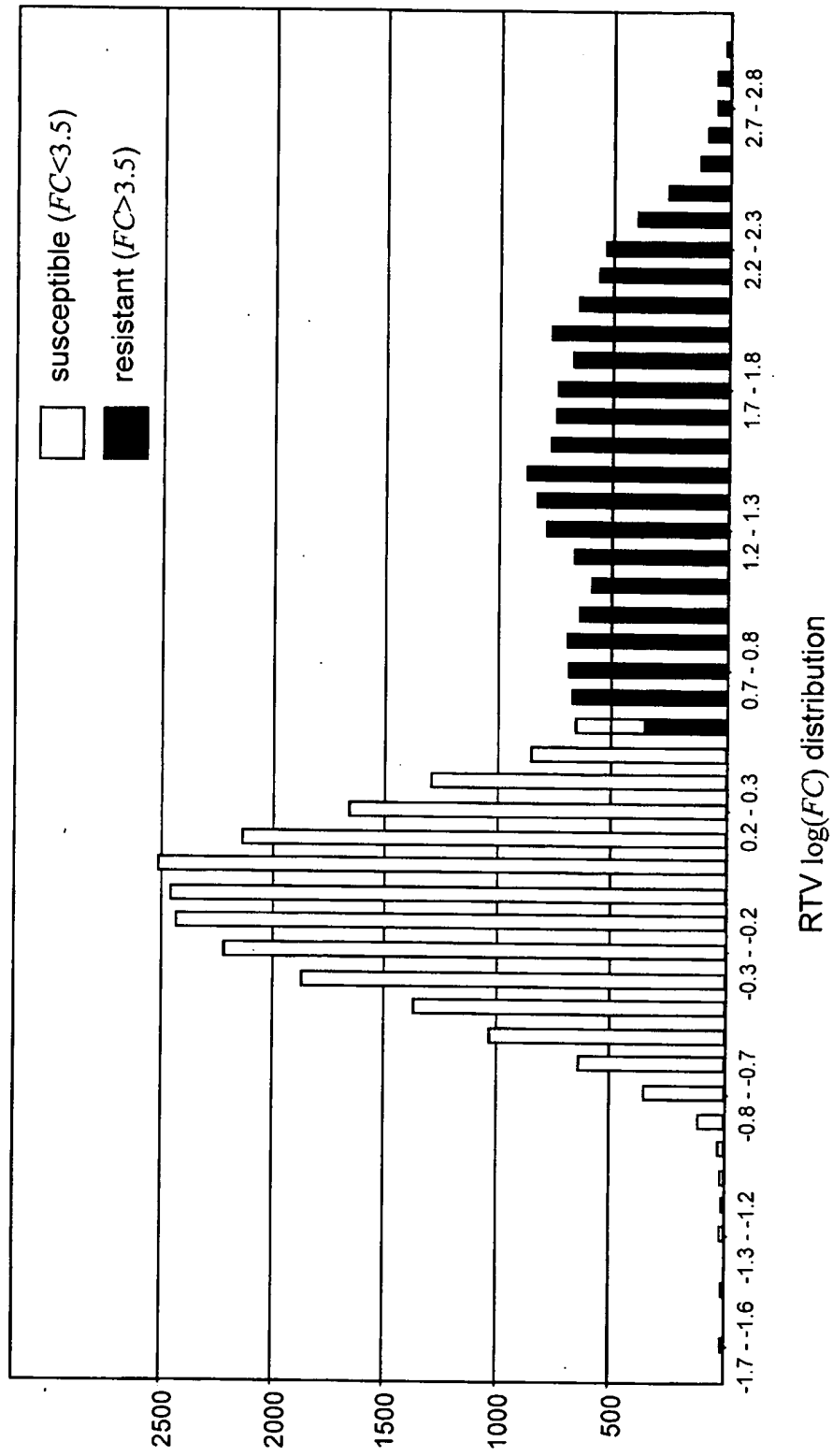


FIG. 3

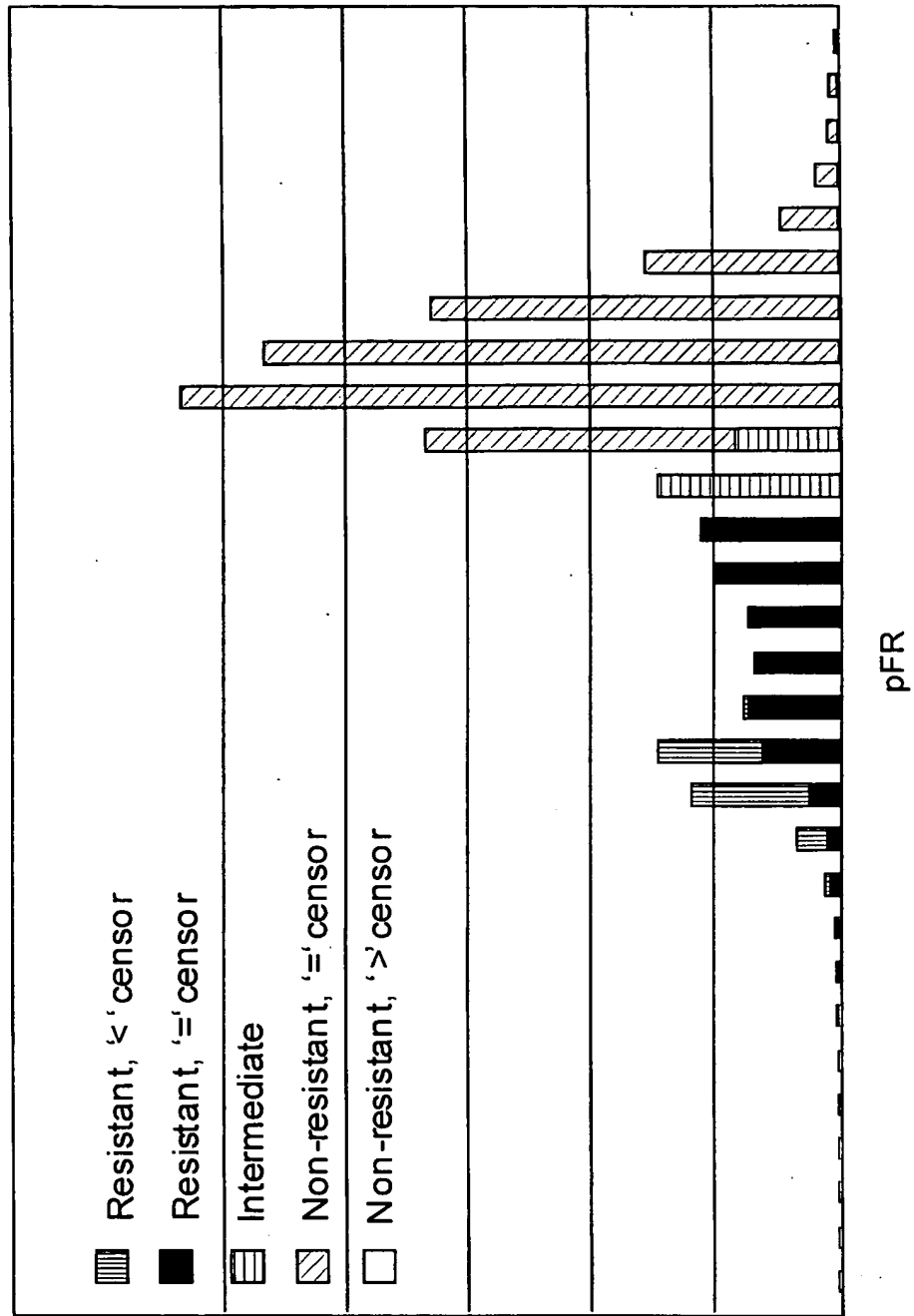


FIG. 4

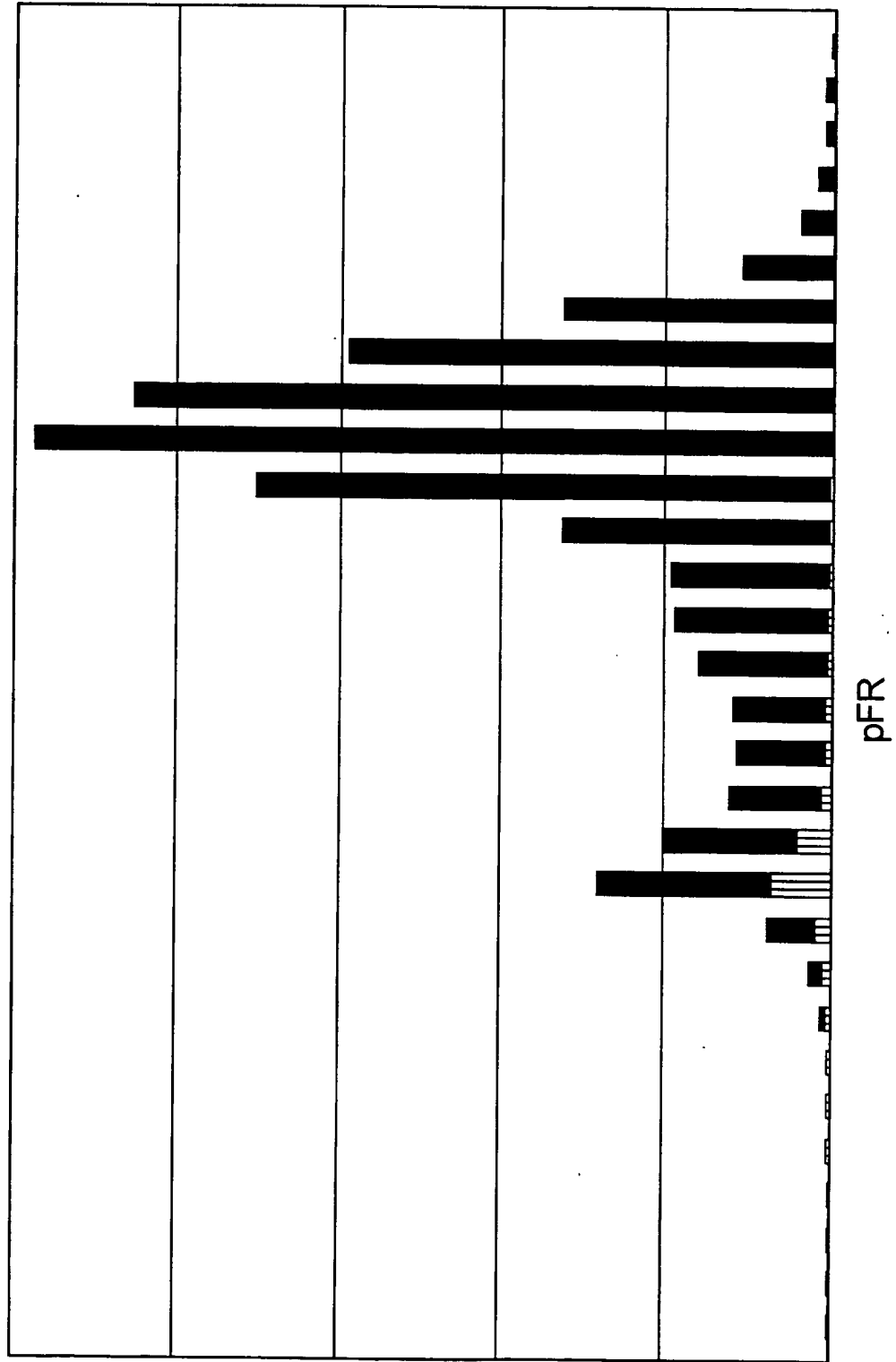


FIG. 5

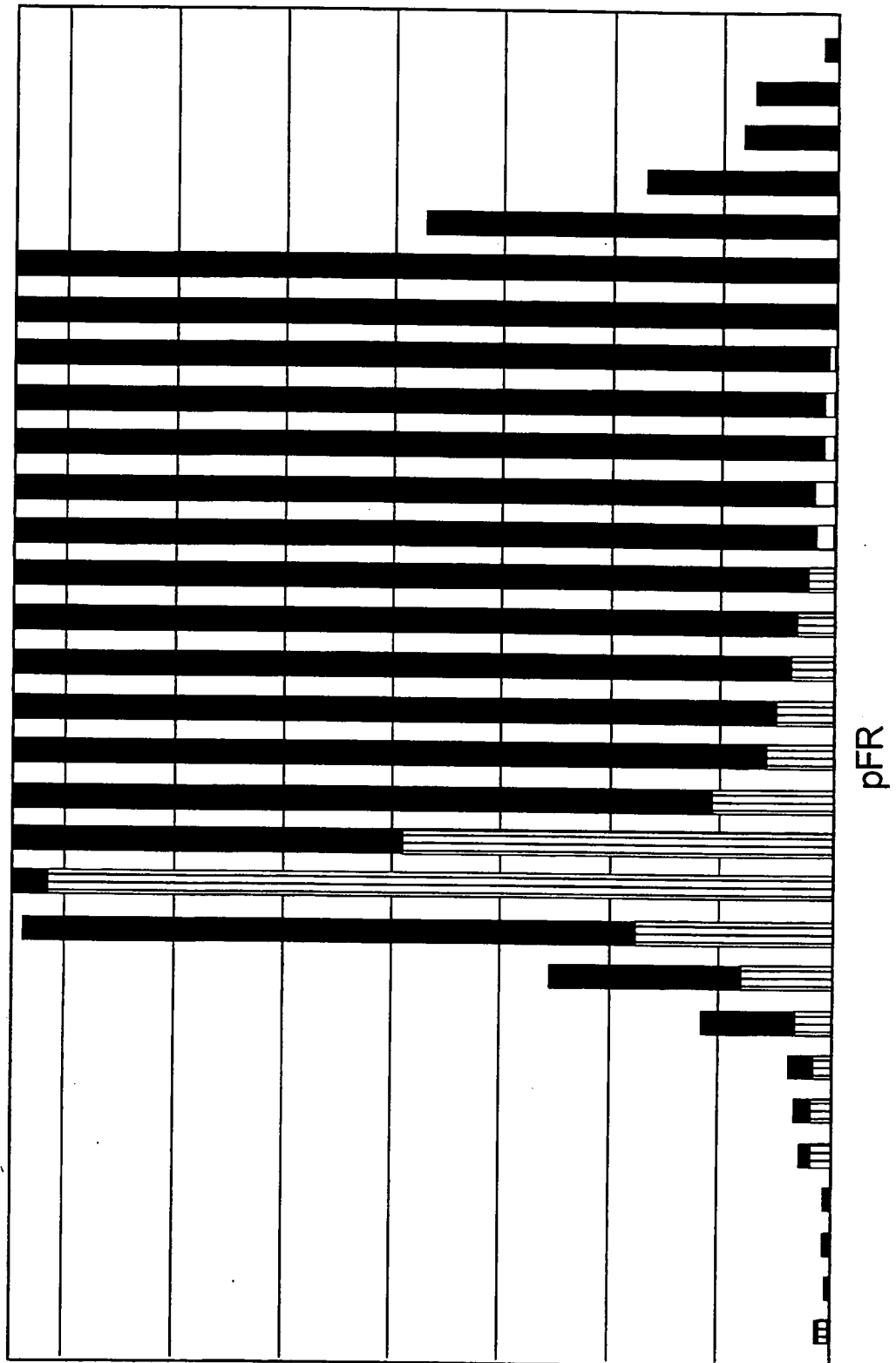


FIG. 6

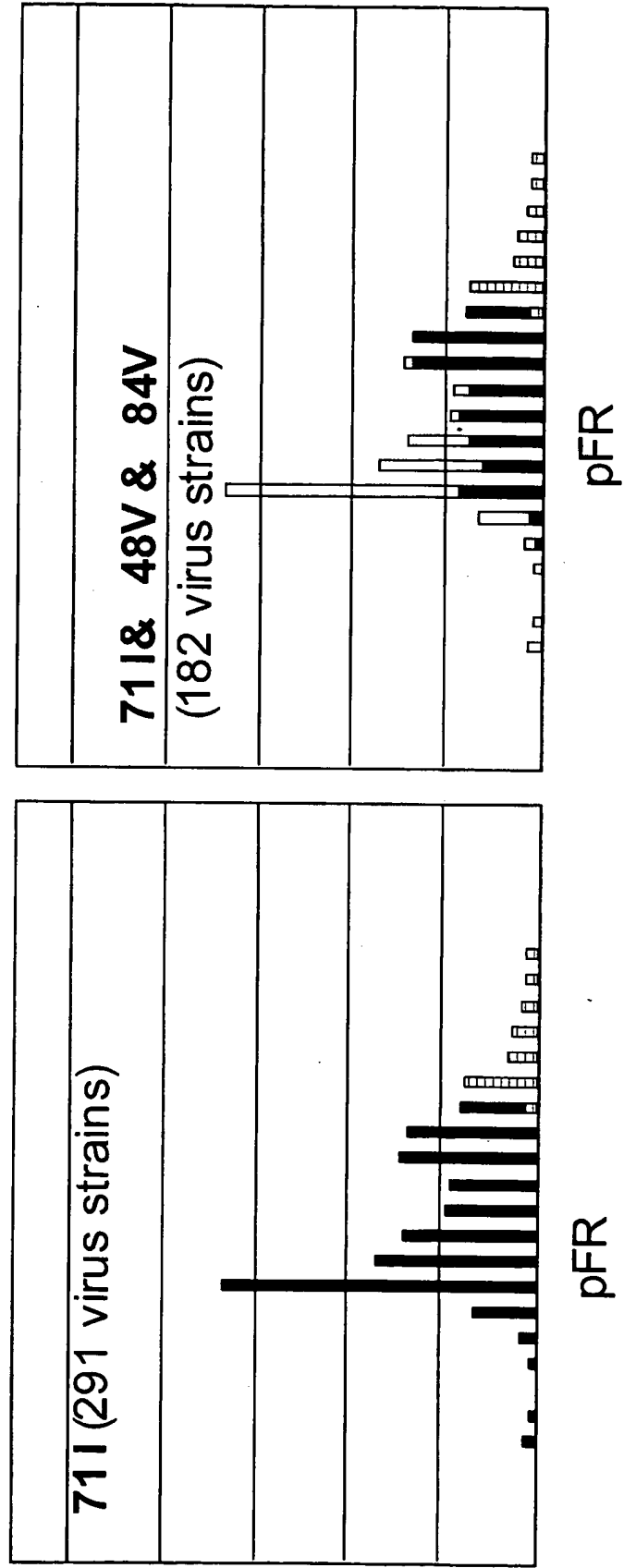


FIG. 7

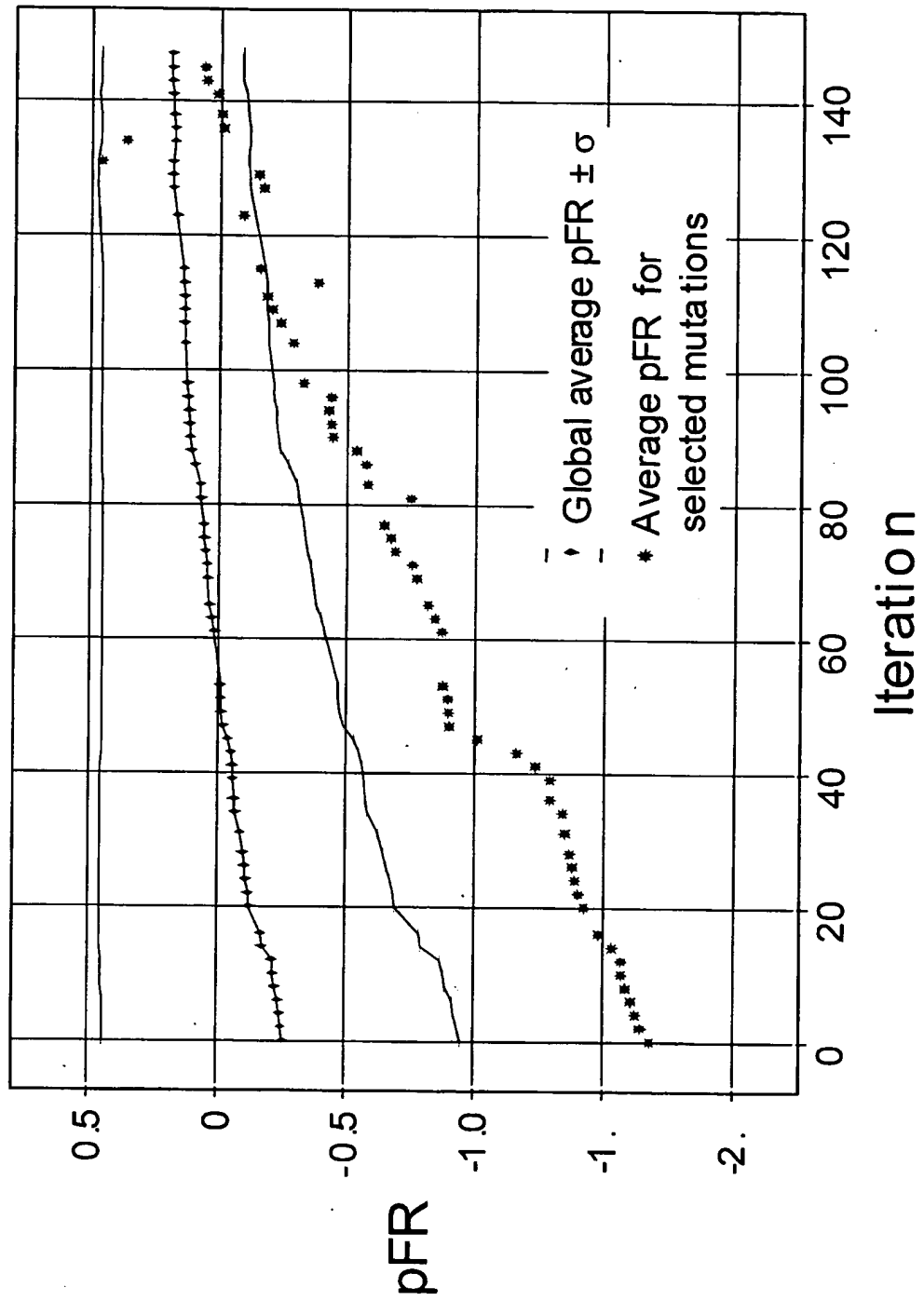


FIG. 8

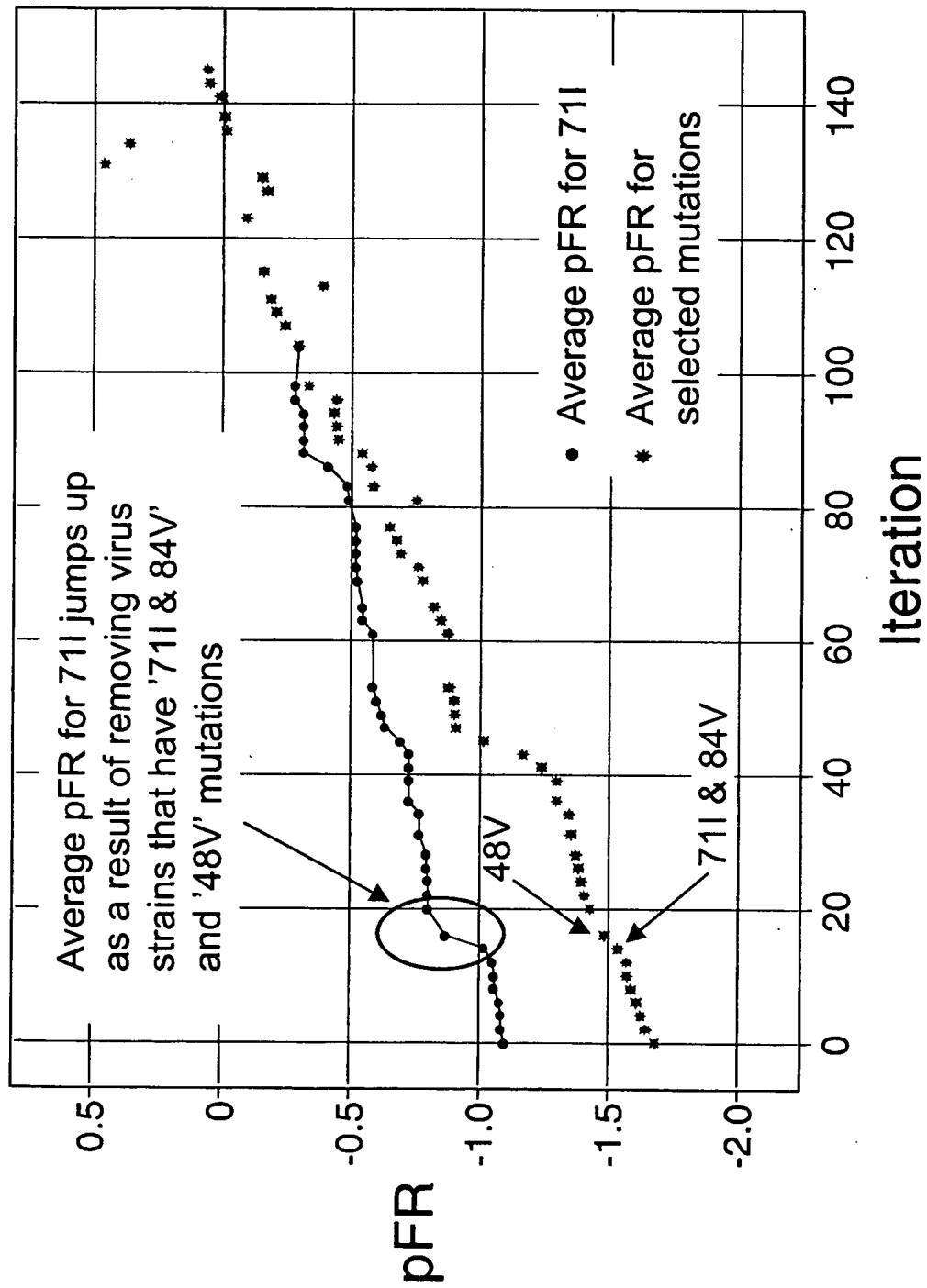


FIG. 9

Sample		3	10	12	15	19	20	24	30	32	36	37	41	46	48	54	62	63	71	74	75	77	82	84	93	
		Position																								
V1	I									IV	N	I					P						A		L	
V2	I	I		V		R					I	N	K		V	T		T	V	A			A		L	
V3	I		S	I				N				N					V	P			I	I			L	
V4	I						I					N	I/M		IV		P	V					T	IV		

FIG. 10

Regression model		Virus sample			
Mutation	log(FC) shift	V1	V2	V3	V4
L24I	0.50				1
L30N	0.39			1	
32I	0.32	1/2			
46I	0.21	1			1/2
54V	0.52		1		
82A	0.63	1	1		1/2
82I	0.59				1
84V	0.67				1/2
Other interactions		-0.14	0.22	-0.17	-0.02
predicted log(FC)		0.86	2.18	-0.56	0.61
measured log(FC)		0.89	2.19	-0.50	0.61

FIG. 11

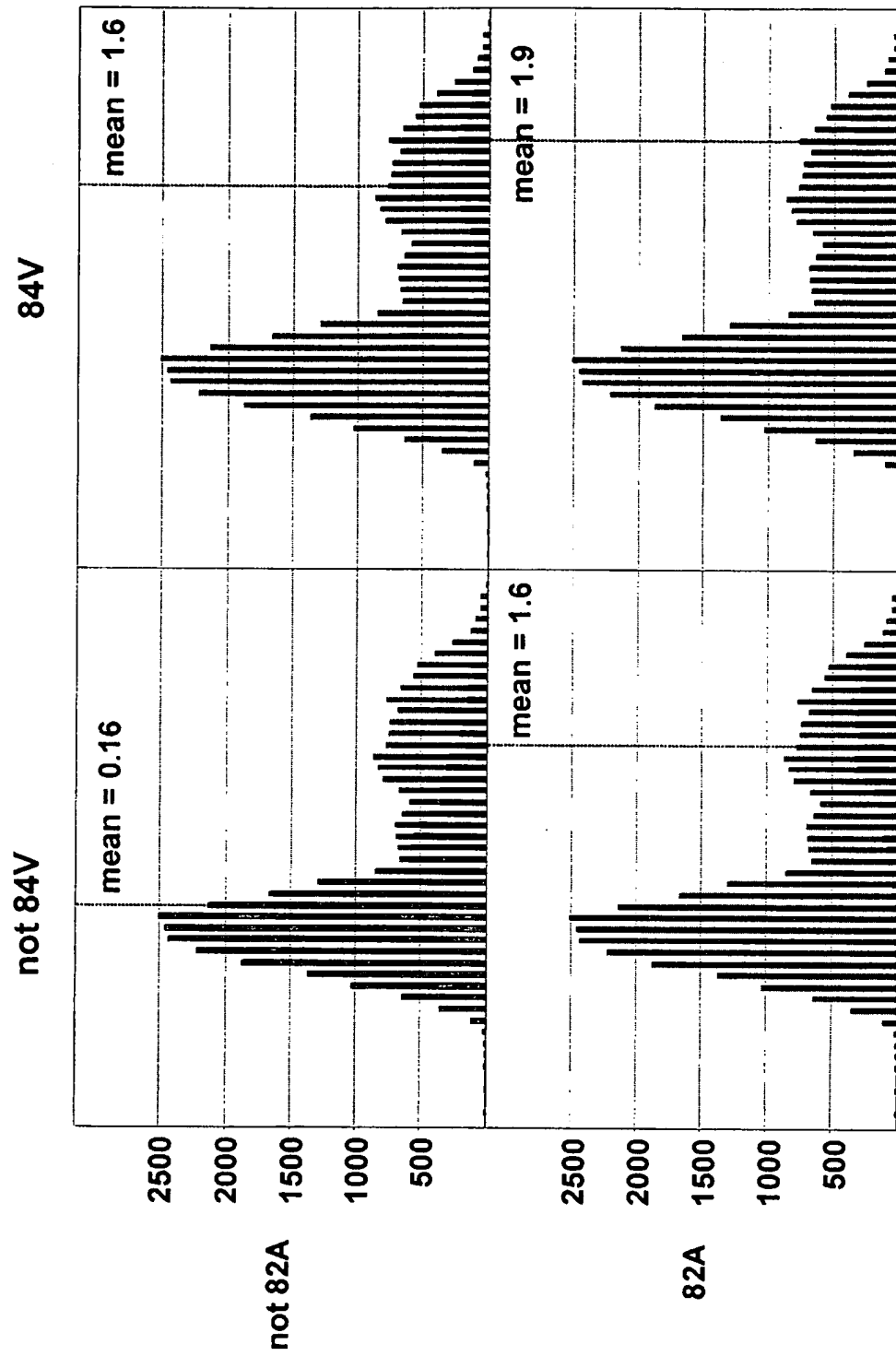


FIG. 12

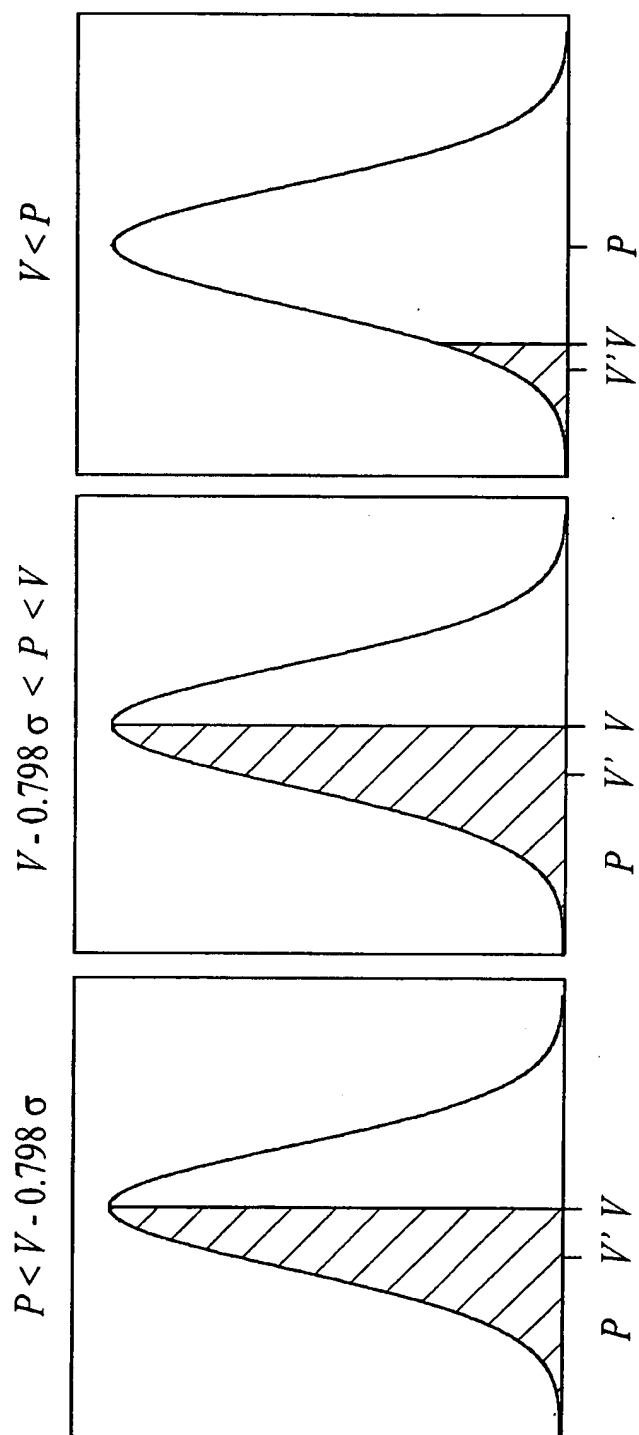


FIG. 13

Mutation	1 st order log(FC) shift	Prevalence in dataset
10I*	2 nd order terms only	9,707
10R	0.35	106
10V*	0.15	1,269
20M	2 nd order terms only	436
20R*	2 nd order terms only	2,093
32I	0.32	845
33F*	2 nd order terms only	1,074
36I*	2 nd order terms only	8,473
46I*	0.21	4,115
46L	0.19	1,745
54L	0.33	367
54V*	0.52	4,553
71T	2 nd order terms only	2,611
71V	2 nd order terms only	7,261
82A*	0.63	4,886
82F	0.92	290
82T*	0.59	642
82S	1.17	120
84V*	0.67	3,558
90V*	0.38	9,609

FIG. 14

Mutation	$\log(FQ)$ shift	Prevalence in dataset
24I	0.50	1,027
30N	-0.39	1,715
54T	1.33	155
73C	0.45	357
73S	0.38	2,224
73T	0.53	559
82M	0.66	33
84A	1.73	70
84C	0.79	67

FIG. 15

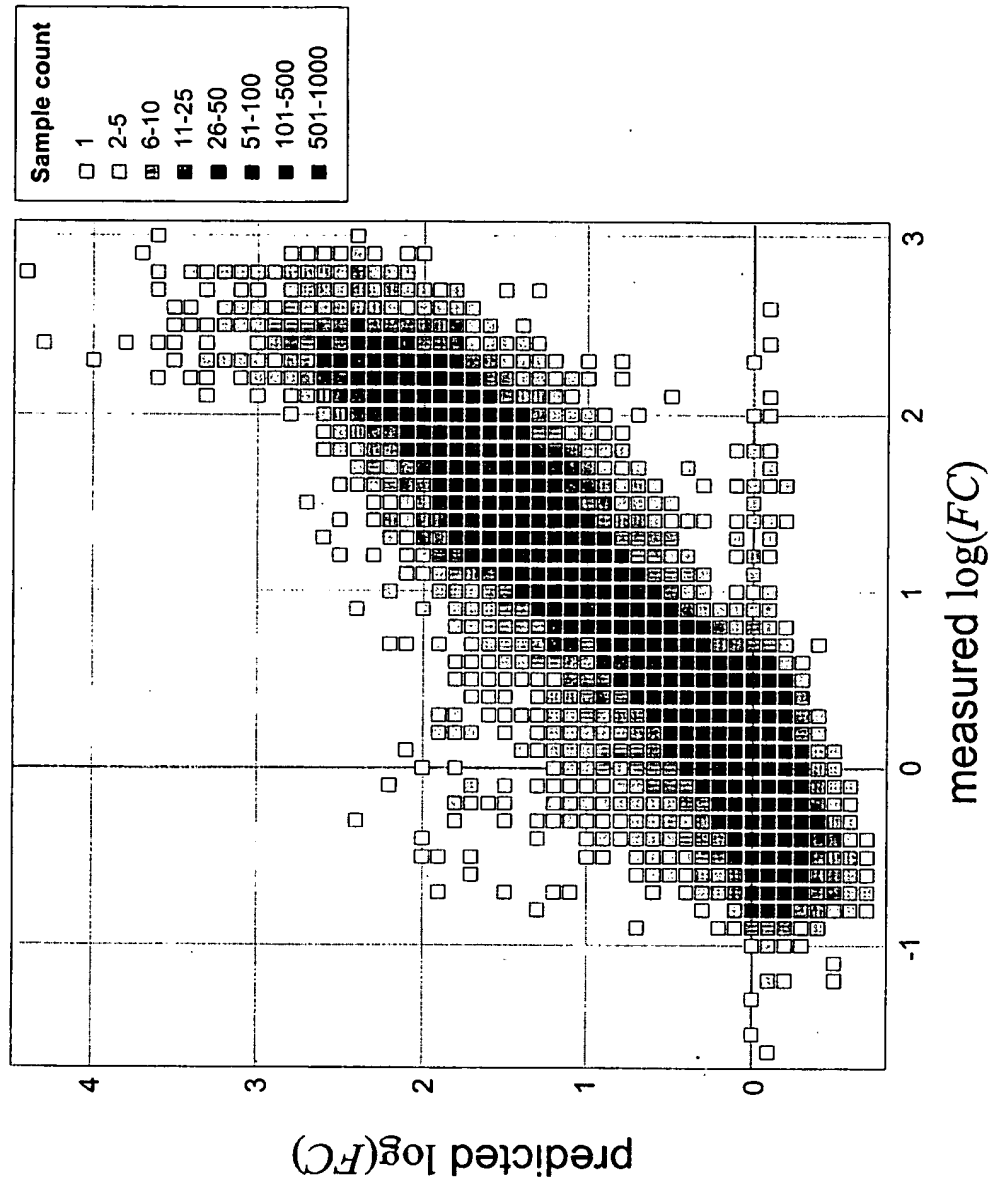


FIG. 16

	Nr. of samples	Resistant fraction (FC>3.5)	Leave-one-out prediction error	Sensitivity	Specificity
Decision tree	469	50.1%	10.2%	89.8%	89.7%
Linear model	469	50.1%	6.4%	92.9%	94.4%
Linear model	34,502	38.3%	5.6%	93.0%	95.4%

- Regression model identifies 53 single mutations and 96 pairs of mutations as having a positive or negative contribution to RTV susceptibility
20 out of 22 mutations from IAS list⁽¹⁾ are confirmed to be significant by regression model

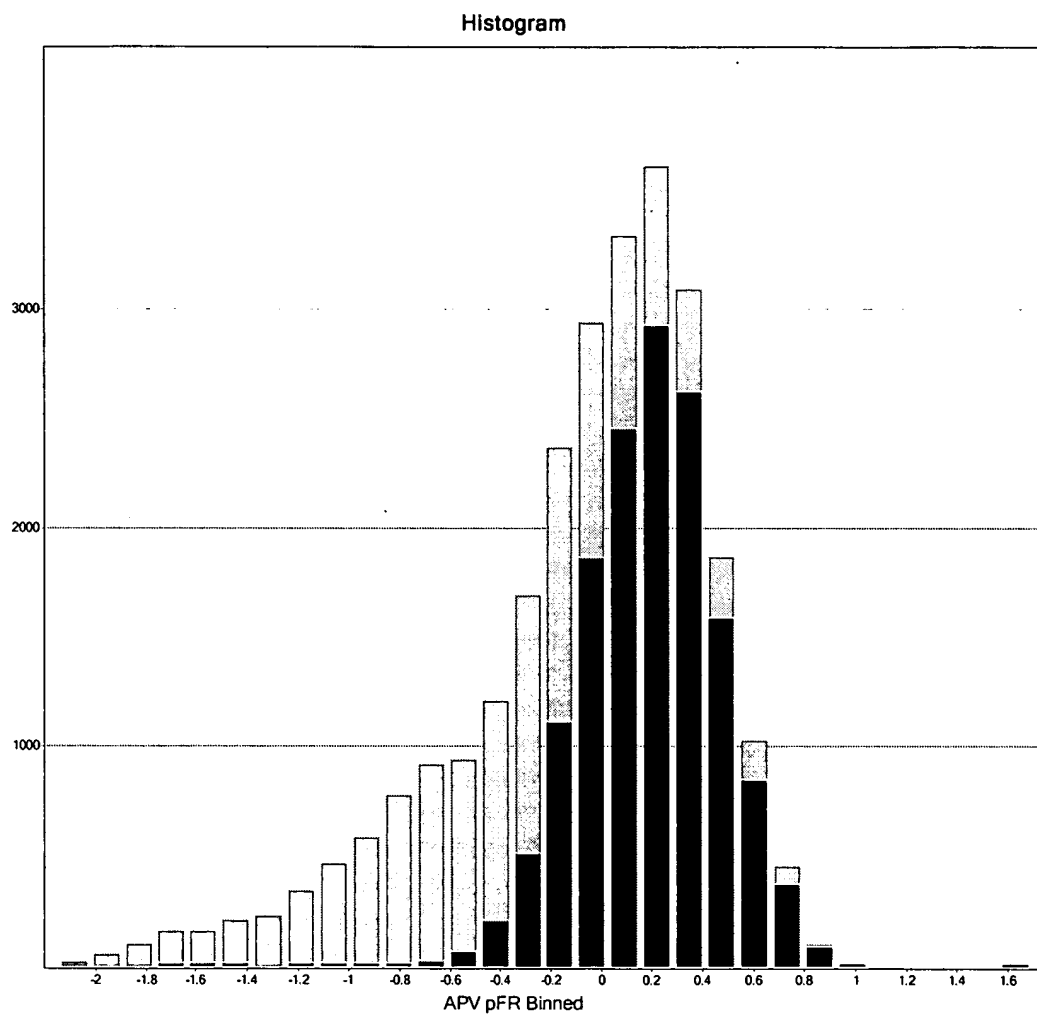


FIG. 17

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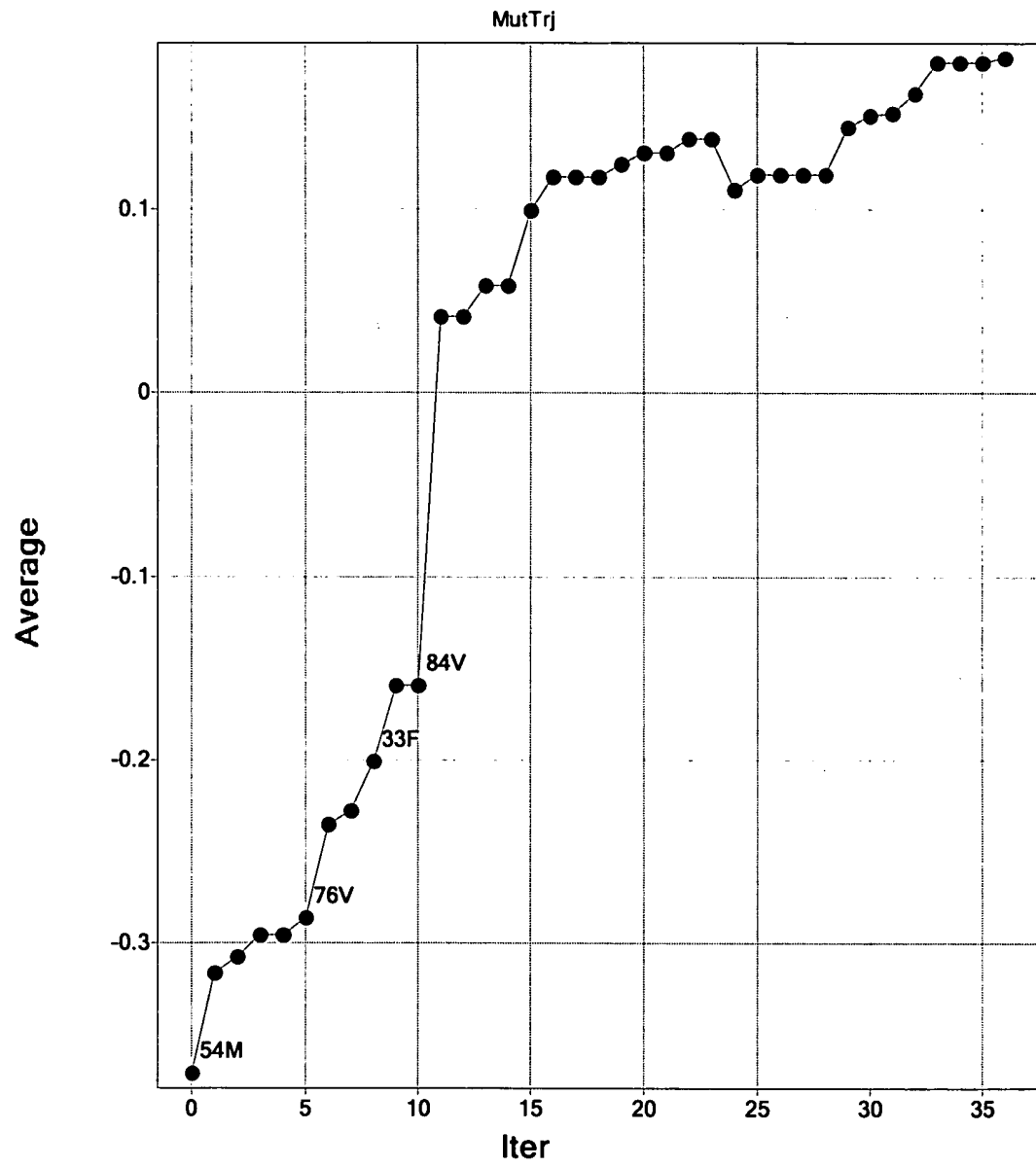


FIG. 18

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Scatter Plot

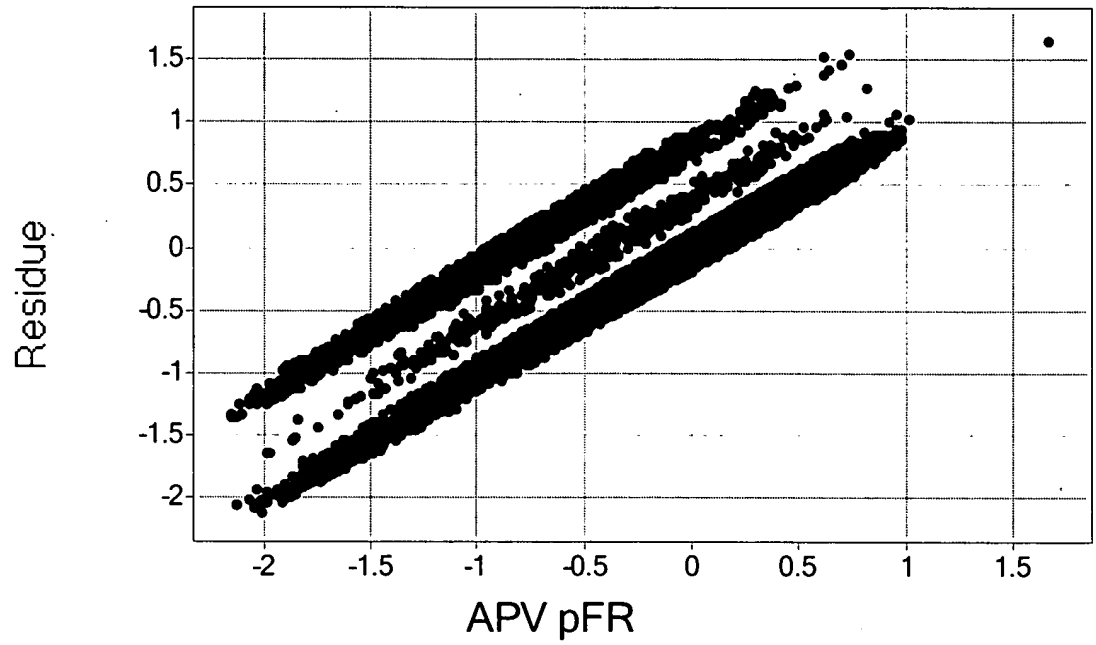


FIG. 19

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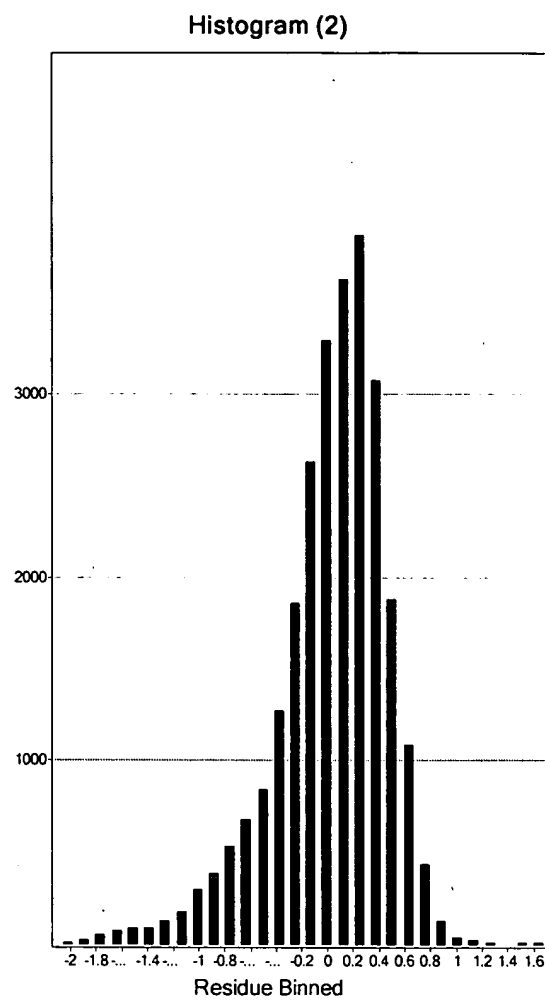


FIG. 20

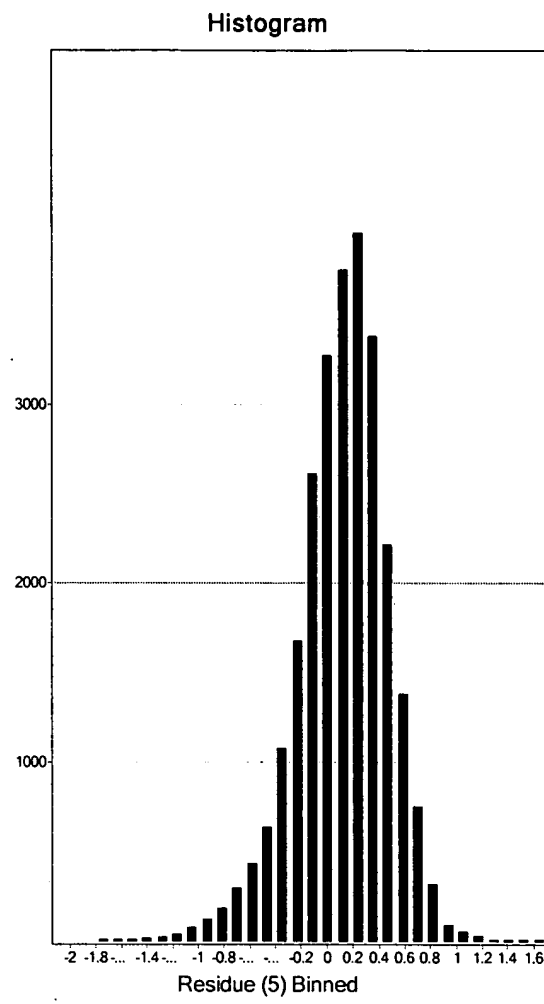


FIG. 21